

Scientific Institute of Public Health

Unit of Epidemiology

Case Control study among schoolchildren

on the incident related to complaints following the consumption of Coca-Cola Company products,

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This study was performed by the unit of epidemiology of the Scientific Institute of Public Health.

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1. Executive Summary

Background: In June 1999, an outbreak of complaints potentially related to the Coca Cola Company products was first reported in school setting in Belgium, and subsequently in the general population of Belgium and France. No toxic cause being yet established, a mass psychological illness (MSI) was hypothesised.

Methods: We performed a case control study in the five schools where the outbreak started. School children were considered as cases if they had had, on the day of the outbreak, at least one of the following complaints: headache, nausea, vomiting, abdominal pain, trembling, dizziness or diarrhoea. Controls were selected among children from the same class, whose names were next on the alphabetical list. The investigation included a face-to-face interview and a review of medical records. Two different production sites supplied soft drinks for Bornem and for the other schools. Analyses were done separately.

Results: Between the 8th and the 20th June, Poisons Call Centres reported over 1000 calls, for which 50% mentioned complaints related to Coca Cola Company products. All cases in the general population occurred after the first outbreak in the school in Bornem on the 8th and the 9th of June, and after extensive media coverage. In the schools involved, questionnaires of 112 (99 females) cases and 165 (129 females) controls were completed. Headache (62.5%), abdominal pain (56.3%) and nausea were the main complaints.

In the school in Bornem, 34 out the 37 cases and 8 of the 34 controls had consumed at least one Coca-Cola soft drink (OR=36.8, 95%Cl 7.6-207.4). Delay between Coca-Cola consumption and occurrence of symptoms ranged from 20 to 1230 minutes (median = 3 hours). Toxicological analysis revealed the presence of hydrogen sulphide that explains the "off" odour.

In the other schools, 31 out the 75 cases and 22 of the 130 controls had consumed at least one Coca-Cola soft drink (OR=3.5, 95%CI 1.7-7.0). Delay between Coca-Cola consumption and occurrence of symptoms ranged from 0 to 465 minutes (median =2 hours).

Conclusion: The outbreak represented a significant public health problem in terms of the number of people affected and resources mobilised. Although it seems reasonable to attribute the first cases in Bornem to Coca-Cola consumption, we cannot prove nor exclude a MSI in the other schools where the outbreak took place after media coverage.

The Coca-Cola consumption hypothesis was supported by a high risk of illness for students exposed to regular Coca-Cola consumption. The strong association with a bad smell, a similar risk for girls and boys, the lack of classical MSI trigger amplifier present or occurring "in line of sight" (the first students came from different classes and did not see each other getting ill) and the lack of other risk factor, i.e. SF36, also supported this hypothesis in Bornem. The MSI hypothesis could be supported by considering the identified gas in the Coca-Cola as a trigger factor and responsible for anxiety, stomach upset, and perhaps other anxiety symptoms. Classical risk factors of MSI were also present. The first outbreak occurred in a school with a high proportion of teenager girls. The context of stress caused by the food security scare following the dioxin crisis, the upcoming elections and end examinations were cumulative risk factors.

Recommendations: More co-ordinated toxicological analyses, either on the soft drinks or on the blood samples should have been performed, and the ones performed should have been performed earlier in order to identify more than only residual concentrations of potential toxic substances and should have been performed by neutral laboratories. Criteria for early detection of MSI outbreaks are needed for public health professionals in the community.

A reflection on the involvement and improvement of the application of epidemiological tools as soon as possible in the management of such events should be done. As in many other countries, a central intervention epidemiology unit should receive the initial request to investigate. Intervention epidemiologists are trained to respond and co-ordinate these investigations. The Epidemiology Unit of the Scientific Institute of Public Health has the resources and the capacity to develop this, but lacks the mandate to develop intervention epidemiology. The mandate includes a clear, legally defined, task to tackle crises in public health. This mandate should be issued pro-actively (and not when a crises

occurs) and supervised by all the different (public health) authorities. To allow an immediate response, a contact person within each of these authorities should be defined. To allow supervision, a supervisory body should be installed, a role which could be taken by the High Council of Health.

2. Introduction

On June 8th 1999, an outbreak of health complaints (nausea, vomiting, abdominal pain, malaise) potentially related to the consumption of glass bottled Coca-Cola consumption, occurred in a school in Bornem, Belgium. The majority of the students were taken to the hospital. The 10th, 11th and 14th June, outbreaks with the same but weaker complaints occurred in four other schools (Brugge, Harelbeke, Kortrijk and Lochristi). Between the 8th and the 20th June, the Poisoning Call Centre (PCC) reported over 1000 calls, for which 50% mentioned complaints related to Coca-Cola consumption and 50% asked for information [1]. Two different Coca-Cola production sites were suspected.

Coca-Cola Company rapidly reacted and recalled the suspected lot in Bornem from the market the 9th of June. Different providers supplied the Coca-Cola products of the schools. The production plant of Antwerp supplied the Coca-Cola products of Bornem; the Dunkerque plant in France supplied those of Brugge and Lochristi. The production plant of Dunkerque and Gent supplied the Coca-Cola products of Harelbeke. The supplier of Kortrijk was unknown.

Coca-Cola Company announced on 15 June that they had identified two causes for those outbreaks. In both cases, the symptoms were attributed to a trigger factor (an off odour) responsible for a mass sociogenic illness (MSI). In Bornem, the off odour in the glass bottle of regular Coca-Cola was attributed to the presence of carbonyl sulphide, contaminating carbon dioxide, and hydrogen sulphide. In the other schools, a fungicide applied on transport pallet had contaminated the outside of some cans from the production plant of Dunkerque. A chemical reaction between this fungicide and the chlorinated products used to clean automatic dispensers could provide the methyl-cresol that was also considered to be responsible for a foul odour and taste. In both cases, the toxicological analyses from Coca-Cola Company concluded that the very low concentration of both incriminated substances could not cause any toxicity.

The different outbreaks occurred in the midst of the dioxin crisis, just before the elections and at the end-examination period. On June 18, ten days after the onset of the symptoms, the Ministry of Public Health of Belgium contacted the Institute of Public Health (I.P.H.) and asked for a meeting to be held on June 21st in order to discuss the Coca-Cola incident.

Following that meeting, as the evidence for the 2 different causal models proposed by Coca-Cola Company did not convince the Ministry of Public Health, the Epidemiology Unit of the IPH was asked to start an investigation in order to infirm or confirm the epidemiological link with the Coca-Cola products.

In this study, we aim to identify the origin of those outbreaks performing an epidemiological investigation, which results should be confronted to the toxicological results.

3. Objectives

The objective of the study was to identify the cause(s) of those outbreaks.

4. Hypotheses

The study was based on two hypotheses:

- 1. The consumption of Coca-Cola products was responsible for the health complaints.
- 2. Mass sociogenic illness (M.S.I.)* was responsible for those outbreaks.

^{*}A mass sociogenic illness [2] also called mass psychogenic illness [3,4] is defined as "the occurrence in a group of people of a constellation of physical symptoms suggesting an organic illness but resulting from a psychological cause, with each member of the group experiencing one or more of the symptoms that can not, however, be explained biologically " [2,3].

5. Method

5.1 Study design

We performed two case-control studies, one with respect to the Bornem outbreak and one with respect to the outbreak in the 4 other schools, in order to test 2 epidemiological hypotheses:

- 1. Cases were more likely than control to consume Coca-Cola Company product
- 2. Cases were more likely than control to be susceptible to a MSI

We expected 2 controls for each case matched on class. In the school in Bornem, only one control for each case was selected.

The case control study was completed with an investigation of the outbreak-scenario of each school.

5.2 Population

Since the first outbreak occurred in a school and although there were many Coca-Cola-related illnesses reported outside of a school environment, it was more practical to ascertain cases and find suitable controls in a school setting. Thus, cases and controls were selected among students who were present during the days of the outbreak (reference day) occurred in each school of Bornem, Brugge, Harelbeke, Lochristi and Kortrijk.

5.3 Definition of the cases and the controls

A case was defined as a student, who reported on the reference day (the first day of the outbreak in the school involved) or the following day, at least one of the following complaints: nausea, vomiting, abdominal pain, diarrhoea, trembling, headache or dizziness.

Controls were students from the same class, next on the alphabetical list (descending order), present on the reference day and the following day and who were not sick in the two weeks preceding the reference day until the end of the following day.

5.4 Sample size

The calculation of sample size was guided by the current number of cases, the need for sufficient power and the practical feasibility to obtain information on all cases and control within a two-day period.

5.5 Case finding

Case finding was performed among students who complained to the directors of the schools.

5.6 Data collection

Following the initial request by the Ministry of Health on June 21st, the study was designed on June 22nd, while questionnaires were prepared and appointments were made with the school principals. The interviews with the students in the schools were conducted on the 23rd, 24th and 25th of June. All data from those interviews were entered in a database on June 25th, and a preliminary analysis allowed a first report to be made by June 28th.

5.6.1 Interviews of the students

A standardised questionnaire was completed in schools during a face to face interview in the schools of Bornem, Brugge, Harelbeke and Kortrijk. The students were grouped and managed by an interviewer when completing the questionnaire in Lochristi. The interviews flowed in a setup that allowed exposure information to be collected blinded regarding the case/control status. The following data were collected (annex 1):

- Demographic data (gender, age)
- Food consumption (place, time)
- Beverage consumption the day of the outbreak occurred (place, time, package, particular characteristic)
- Symptoms noted by the students (time, type)
- Having friend(s) who reported to be ill at the reference day
- o Questions on mental health (SF36).

Thirteen trained interviewers collected information in the 5 schools on the 23, 24 and 25 of June.

5.6.2 Data collection from medical charts

An abstract form was developed to collect information from medical records of students who went to the emergency unit or were hospitalised (annex 2).

5.7 Information from the physicians

Physicians who took care of the patients in the hospitals completed a qualitative and open questions of a standardised questionnaire. The collected information concerned the ambience and the behaviour of the students. Also their feeling about a possible organic cause responsible for the diseases was questioned (annex 3).

5.8 Information on the scenario in schools

An interview by telephone with the directors of the five schools allowed having information concerning the scenario of the outbreak; i.e., how was the alert made? Who was contacted? How many students had health complaints? What was the process to identify students with health complaints? What were the criteria to refer student(s) to an emergency unit?

5.9 Analysis

The glass bottles of the Bornem school were provided by one Belgium plant and the plastic bottles and cans to the other schools were provided by other production plants. Therefor, it was decided to analyse separately the data from Bornem and those from the other schools. Descriptive analysis and calculation of the Odds of the exposure among cases and controls were performed with EPI INFO version 6.04c and multivariate analyses with SPSS, version 8.0.

An analysis of the data collected by the poisoning call centre is not included in this report. Data of the media (written, TV, radio) were collected but have not yet been analysed.

6. Toxicological information

Epidemiological results were confronted with toxicological results of the different laboratory report that have analysed several Coca-Cola products.

We also have the results of the laboratory analysis ordered by the Food Inspection of the Ministry of Public Health.

7. Attack rate and epidemic curve

7.1 Attack rate and epidemic curve in Bornem

In Bornem, the outbreak occurred the 8th June and the 9th June. Thirty-seven students among the 280 were identified as cases and the attack rate (AR) was 13.2%. The AR was 15.6% (28/179) among girls and 8.9% (9/101) among boys (RR= 1.8; 95%CI: 0.9-3.6). The mean age of the cases was 13 years, the median was 13.5 years (min. 10, max. 17).

Thirty-one cases occurred on 8th and 6 occurred on the morning of 9th June. The median of occurrence was at 3 p.m. on 8 June (figure 1).

No cases were observed among the school staff.





7.2 Attack rate and epidemic curve in the other schools

In the other schools, outbreaks occurred on three different days, 10th June in Brugge, 11th June in Harelbeke and 14th June in Lochristi and Kortrijk. Seventy-five cases occurred among the 2055 students of the 4 other schools. The AR was 3.6%. The AR was lower than in Bornem. The AR was 4.3% (72/1666) among girls and 0.7% (3/394) among boys (OR= 5.7; 95%CI: 1.8-17.9). The mean age of the cases was 14 years; the median was 15 years (min. 13, max. 19).

Seventy-two cases occurred on the first day of the outbreak and 3 occurred on the following day. Except in Lochristi, the spreading of cases was larger than in Bornem (Figures 2, 3, 4, 5).

Figure 2 - Cases by time of onset, Brugge, Belgium, 1999.

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Figure 3 - Cases by time of onset, Harelbeke, Belgium, 1999.



Figure 4 - Cases by time of onset, Kortrijk, Belgium, 1999.



Figure 5 - Cases by time of onset, Lochristi, Belgium, 1999.



8. Symptoms

8.1 Symptoms of the students of Bornem

Abdominal pain, headache, nausea, respiratory problems, trembling and dizziness were the principal complaints collected from the medical records (Table 1). The number and the variability of the symptoms notified by the students were more important than those identified by medical records.

Respiratory problems were more frequently reported among the students of Bornem (25.0%) than among the students of the other schools (4.8%) (p=0.01) (Table 13 and 15), explaining the requested chest-radiography.

Clinical examination was normal for 27 cases except an extreme pallor for the first cases. For 3 patients, a sensitive abdomen or staggering was noted. For 2 patients, medical data were unknown.

Among the 37 cases identified in Bornem, 32 went to the emergency unit. 12 were hospitalised at least one night.

Twenty students went to the emergency unit with a private car. There were 12 missing data for this variable. None of the cases went to the hospital by ambulance.

Among the 32 students who went to the emergency unit, 22 came from school, 3 from home and for 7 data were not available.

All symptoms disappeared spontaneously without specific treatment for 25 students. Seven cases received a symptomatic treatment (glucose, oxygen, antalgic, and aerosol).

Six students came back within a few days for a consultation because of persistence of symptoms.

Table 1 - Symptoms collected from the students and from the medical records, Bornem,Belgium 1999.

Symptoms	Medical information (%)	Student information (%)	
	n = 32	n = 37	
Headache	20 (62.5)	33 (89.2)	

Abdominal pain	18 (56.3)	35 (94.6)
Nausea	13 (40.6)	29 (78.4)
Respiratory troubles	8 (25)	5 (13.5)
Trembling	7 (21.9)	32 (86.5)
Dizziness	7 (21.9)	26 (70.3)
Asthenia	7 (21.9)	1 (2.7)
Weakness	3 (9.3)	6 (16.2)
Other	23 (71,9) *	36 (97.3) **

Patients had more than one symptom.

^{*} Asthenia, myasthenia, troubles of the visual acuity, scotoma, backache, painful throat, handtingling, drowsiness, vomit, diarrhoea, malaise, palpitation.

** Malaise, vomit, diarrhoea, troubles of sleep, troubles of the visual acuity, hand-tingling.

We compared the symptoms of the first 12 cases (before 2h00 p.m.) to the symptoms of the other students to look after the severity and the difference between the 2 groups. The proportion of the main symptoms (headache, nausea, abdominal pain, dizziness and trembling) was higher among the first 12 cases than among later cases. Trembling characterised more frequently the later other cases than the first 12 cases (Table 2).

Table 2 - Symptoms of the first cases compared to the symptoms of the following cases, data from the medical records, Bornem, Belgium 1999.

Symptoms	First cases (%) n = 12	Other cases (%) n = 20
Headache	10 (83.3)	10 (50.0)
Nausea	8 (66.7)	5 (25.0)
Abdominal pain	7 (58.3)	11 (55.0)
Dizziness	4 (33.3)	3 (15.0)
Trembling	1 (8.3)	6 (30.0)
Respiratory troubles	4 (33.3)	4 (20)
Asthenia	3 (25)	4 (20)
Weakness	0	3 (15)

Patients had more than one symptom.

8.2 Symptoms of the students of the other schools

Headache, abdominal pain, nausea, dizziness and trembling were the principal complaints identified through the review of medical records. During the interview students more frequently notified symptoms than were collected from the medical records,

particularly dizziness and trembling (Table 3).

Few students complained of leg pain, myalgia or muscles cramp.

Clinical examination was normal for 56 cases. For 6 patients, flush and/or red eyes were noted.

Among the 75 cases identified in the other schools, 62 went to the emergency unit, 12 were hospitalised at least one night (7 one night, 4 two nights and 1 three nights).

Twenty-three students went to the emergency with an ambulance and 4 with a private car. For 35 cases, data for this variable were missing.

Among the 62 hospitalised cases, 26 came directly from school, 1 from home and for 35 this information was not available.

All symptoms disappeared spontaneously without specific treatment for 44 students. Thirteen cases received a symptomatic treatment (glucose, antalgic, and "PrimperanÒ" for abdominal discomfort).

A few days later, 2 students came back for consultation because of persistence of symptoms.

Symptoms	Medical information (%) n = 62	Student information (%) n = 75
Headache	48 (77.4)	67 (89.3)
Abdominal pain	39 (62.9)	68 (90.7)
Nausea	36 (58.1)	66 (88)
Dizziness	19 (30.6)	41 (54.7)
Trembling	18 (29)	60 (80)
Respiratory troubles	3 (4.8)	2 (2.7)
Weakness	3 (4.8)	9 (12)
Other	61 (98.4) [*]	62 (86.7) **

Table 3 - Symptoms collected from the students ' interviews and from the medical records, Other schools, Belgium 1999.

Patients had more than one symptom.

Loss of appetite, neck pain, myalgia, back pain, flush, feel hot, shiver, anxiety, red eyes, malaise, somnolence, transpiration, feeling warm or cold or hot, loss of consciousness, vomiting, diarrhoea,.

^{**}Arm tingling, back pain, neck pain, palpitation, feeling cold/hot, eyes pain, myalgia, loss of the visual acuity, throat pain, vomiting, diarrhoea, blood in stool, malaise.

9. Results of the case-control study

In Bornem, thirty-seven cases were identified and 34 controls were selected. Cases and controls were similar for age and gender.

In the other schools, seventy-five cases were identified and 130 controls were selected. The proportion of girls among the cases (96.0%) was superior to the proportion (84.6%) among the controls (p = 0.01). Cases and controls were similar for age.

9.1 Odds of exposure to regular Coca-Cola consumption in Bornem

Among the 37 cases, 34 (91.9%) had consumed regular Coca-Cola at school on the day of the outbreak occurred compared to 8 of the 34 controls (OR = 36.8; 95% CI: 7.6-207.4) (Table 4).

9.2 Odds of exposure to regular Coca-Cola consumption in the other schools

Among the 75 cases, 31 (41.3%) had consumed regular Coca-Cola at school on the day of the outbreak occurred compared to 22 of the 130 controls (OR = 3.5, 95% CI: 1.7-7.0) (Table 4).

Table 4 - Odds of exposure to regular Coca-Cola bought and consumed at schoolin Bornem, Belgium 1999.

		BORNEM			
		Cases	Controls (n=34)	OR	95% CI
		(n=37)			
Exposure to	yes	34 (91.9%)	8 (23.5%)	36.8	7.6-207.4
Cola	no	3 (8.1%)	22 (76.5%)		
		OTHER SCHOOLS			
		Cases	Controls (n=130)	OR	95% CI
		(n=75)			
Exposure to regular Coca-	yes	31 (41.3%)	22 (16.9%)	3.5	1.7-7.0
Cola	no	44 (58.7%)	108 (83.1%)		

9.3 Odds of exclusive exposure to specific beverages in Bornem

We compared the odds of exclusive exposure to a specific beverage (bought and consumed at school) among cases and controls. The reference group was consumption of water only or no consumption at all.

In Bornem, students exposed exclusively to regular Coca-Cola were more likely to report health complaints (OR = 21.5; 95% CI: 3.7-235.5) than those who drank either only water or nothing. There was no association between the reporting of illnesses and the consumption of other specific soft drinks (Table 5).

Table 5 - Odds of e	exclusive exposure	to specific beverages	*, Bornem, Belgium 1999.
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Beverages	Cases	Controls	OR	95%CI
	(n=37)	(n=34)		
Coca-Cola Regular	31	8	21.5	3.7 - 235.5
Fanta	0	9	0	0 - 8.3

Coca light	0	0	-	-
Other Coca products	1	3	1.9	0 - 33.6
Other drinks	0	2	0	0 - 47.2
Water/no drink	2	12	ref	_

^{*} Bought and consumed at school on the reference day

9.4 Odds of exclusive exposure to specific beverages in the other schools

In the other schools, the risk associated (OR=5.5; 95% CI: 2.4-13) with exclusive regular Coca-Cola consumption was weaker compared to Bornem. However, there was also an association with Fanta (OR= 3.5; 95%CI: 1.1-10.9) and Coca-Cola light consumption (OR = 12.4; 95%CI: 2.8-77.9) (Table 6).

Table 6 - Odds of exclusive exposure to specific beverages ^{*}, Other schools, Belgium 1999.

Beverages	Cases	Controls	OR	95%CI
	(n=75)	(n=130)		
Regular Coca-Cola	26	20	5.5	2.4 - 13
Fanta	9	11	3.5	1.1 - 10.9
Coca light	9	3	12.4	2.8 - 77.9
Other Coca products	5	5	4.3	0.9 - 20.2
Other drinks	1	5	0.9	0 - 8.5
Water/no drink	19	81	ref	_

^{*} Bought and consumed at school the day of the outbreak occurred

9.5 Odds of exposure to other risk factors in Bornem

Twenty cases out of the 37 (54.05%) had a low mental health score (OR = 2.4, 95%CI: 0.8-7.3) (Table 7). The school in Bornem did not provided food.

Cases were more likely than controls to notify a bad smell of the beverage (OR =40.2, 95%CI: 7.98 - 407.4) than those who were not exposed (Table 7). The exposure to a bad taste was also associated with the risk of illness. (OR= 26.9, 95%CI: 3.7 - 1206.7) (Table 7).

In Bornem, the bad smell of the regular Coca-Cola was more frequently characterised by the cases as being "nasty, rotten or strange" (Table 8).

Cases were more likely than control to notify a bad smell of the regular Coca-Cola (OR = 10.7, 95%Cl 1.5 - 131) (Table 10).

Strange or rotten tastes were more frequently noted for regular Coca-Cola consumption (table 8).

Table 7 - Odds to exposure to other risk factor, Bornem, Belgium 1999.

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Risk factor	Cases	Controls	OR	95%CI
	(n=37)	(n=34)		
Food provided by school	0*	0*	-	-
Having a friend being ill	36	30	4.7	0.4 - 242.8
Mental SF36 score< median	20**	11**	2.4	0.8 - 7.3
Bad smell	27	2	40.2	8.0 - 407.4
Bad taste	17	1	26.9	3.7 - 1206.7

^{*} Bornem school did not provide food

^{**} 1 missing value among the cases and 2 missing values among the controls

Table 8 – Characteristics of the bad smell noted by cases exposed to regular Coca-Cola, Belgium 1999.

Bad smell	Bornem (47) *	Other schools (49) *
Nasty / rotten	15	1
Bizarre / strange	14	0
Gasoline	4	0
Acid / citric	1	1
Musty	2	0
Other	3	0
Total	39	2

* Number of consumed cans or bottles of regular Coca-Cola

Table 9 - Characteristics of the bad taste noted by cases exposed to regular Coca-Cola, Belgium 1999.

Bad taste	Bornem (47) *	Other schools (49) *
Bizarre / strange	6	0
Nasty / rotten	5	0
Bitter	2	1
Acid / citric	2	4
Other	3	3
Total	18	8

* Number of consumed cans or bottles of Coca-Cola

Table 10 - Odds of experiencing bad smell among students drinking regular Coca-Cola, Belgium 1999.

BORNEM

		Cases (n=34)	Controls (n=8)	OR	95% CI
Experiencing bad smell	yes	27	2	10.7	1.5 - 131.0
	no	7	6		
			OTHER S	CHOOLS	
		Cases (n=31)	Controls (n=22)	OR	95% CI
Experiencing bad smell	yes	2	0	_	-
	no	29	22		

9.6 Odds of exposure to other risk factors in the Other schools

Cases were more likely than controls to belong to the low mental health group (OR = 2.4; 95% CI: 1.3 - 4.5) (Table 11).

In the other schools 6 cases were exposed to a bad smell and none among the controls (Table 5).

The exposure to a bad taste was associated with the risk of illness in the other schools (OR= 21.88, 95%CI 3.06 - 961.49) (Table 11). Citric or rotten tastes were more frequently noted for regular Coca-Cola consumption (table 9).

Risk factor	Cases	Controls	OR	95%CI
	(n=75)	(n=130)		
Food provided by school	6	26	0.3	0 - 0.9
Having a friend being ill	65	101	1.9	0.8 - 4.4
Mental SF36 Score< median	47	54	2.4	1.3 - 4.5
Bad smell	6	0	-	-
Bad taste	11	1	21.9	3.1 – 961.5

9.7 Odds of exposure to regular Coca-Cola stratified by the mental health score (SF36)

9.7.1 Bornem

Among students who had a low mental score (< median) 17 cases (85%) had consumed regular Coca-Cola whereas 2 (18.2%) controls did (OR = 21.7, 95%CI: 2.8 - 308.52) (Table 12).

Among students who had a high mental score (> median) all cases (16) had consumed regular Coca-Cola whereas 6 (28.7%) out of the 21 controls did (p < 0.0001) (Table 12).

Table 12 - Odds to exposure to regular Coca-Cola stratified on the SF36, Bornem, Belgium 1999.

HIGH SF36 (> median)				
Exposure	Cases	Controls	OR	(95%CI)

		(n = 16)	(n = 21)			
Regular Coca-Cola	yes	16 (100%)	6 (28.6%)	¥	-	
	no	0	15 (71.4%)			
	LOW SF36 (< median)					
Exposure		Cases	Controls	OR	(95%CI)	
		(n = 20)	(n = 11)			
Regular	yes	17 (85%)	2 (18.2%)	21.74	2.8 - 308.5	
0000-0010	no	3 (15%)	9 (81.8%)			

Crude_{OR} = 36.8, 95%Cl 7.6 - 207.4; MH_{OR} = 59, 95%Cl 9.12 - 382

9.7.2 Other schools

Forty-seven (63.5%) cases and 54 (41.2%) controls had a low mental score (OR = 2.4; 95%CI: 1.3 - 4.5). There were 3 missing values (one among the cases and 2 among the controls).

Among students who had a low mental score (< median) 18 cases (38.3%) were exposed to regular Coca-Cola consumption whereas 8 (14.8%) controls were exposed to regular Coca-Cola (OR = 3.57, 95%Cl 1.25 - 10.47) (Table 13).

Among students who had a high mental score (> median) 13 cases (48%) out of the 27 were exposed to regular Coca-Cola consumption whereas 13 (17.5%) out of the 74 controls were exposed to regular Coca-Cola (OR = 4.36, 95%Cl 1.49- 12.94) (Table 13).

The odds ratio between the two strata was not statistically different (p = 0.7) as also was indicated by a non-significant interaction term in a logistic model. After controlling for the mental health-score the OR did not change substantially, giving no strong evidence for a confounding effect of the mental health status and the likelihood of reporting health complaints.

HIGH SF36 (> median)					
Exposure		Cases	Controls	OR	(95%CI)
		(n = 27)	(n = 74)		
Regular Coca-Cola	yes	13 (48.1%)	13 (17.6%)	4.4	1.5 - 12.9
	no	14 (51.9%)	61 (82.4%)		
		LOW S	F36 (< median)		
Exposure		Cases	Controls	OR	(95%CI)
		(n = 47)	(n = 54)		
Regular Coca-Cola	yes	18 (38.3%)	8 (14.8%)	3.6	2.3 - 10.5

Table 13 - Odds	to exposure to	regular Co	ca-Cola st	tratified on t	the SF36, 0	Other school	s,
Belgium 1999.							

no 29 (61.7%)	46 (85.2%)		
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Crude_{OR} = 3.5, 95%Cl 1.7-7.0; MH_{OR} = 3.9%Cl: 9.2.0 - 7.7

9.8 Odds of experiencing a low mental health (SF36) stratified on the consumption of regular Coca-Cola

9.8.1 Bornem

Thirty-four (90.1%) cases and 8 (23.5%) controls consumed regular Coca-Cola (p<0.001). There were 3 missing values for the SF36 (one among the cases and 2 among the controls).

Among students who consumed regular Coca-Cola 17 cases (50%) experienced a low mental score whereas 2 (25%) controls experienced a low mental score (OR = 3.1; 95%CI: 0.5 - 35.8) (Table 14).

Among students who did not consume regular Coca-Cola all cases (3) experienced a low mental score whereas 9 (37.5%) out of the 24 controls experienced a low mental score (p < 0.0001) (Table 14).

Table 14 - Odds of experiencing a low mental health (SF36) stratified on the consumption of regular Coca-Cola, Bornem, Belgium 1999.

Exposure		Cases	Controls	OR	(95% CI)
		(n = 34)	(n = 8)		,
Sf36	yes	17 (50%)	2 (25%)	3.1	0.5 - 35.8
< median	no	17 (50%)	6 (75%)		
	No regula	ar Coca - Cola co	nsumption		
Exposure		Cases	Controls	OR	(95% CI)
		(n = 3)	(n = 24)		- ,
Sf36	yes	3 (100%)	9 (37.5%)	-	_
< median	no	0	15 (62.5%)		

Crude_{OR} = 2.4; 95%CI: 0.8-7.3; CMH_{OR} = 5.32, 95%CI 1.06 - 26.65

9.8.2 Other schools

Thirty-one (41.3%) cases and 22 (16.9%) controls consumed regular Coca-Cola (p<0.001). There were 3 missing values for the SF36 (one among the cases and 2 among the controls).

Among students who consumed regular Coca-Cola 18 cases (58.0%) experienced a low mental score whereas 8 (38.0%) controls experienced a low mental score (OR = 2.2, 95%CI: 0.6 - 8.3) (Table 15).

Among students who did not consume regular Coca-Cola, 29 (67.4%) out of the 43 cases experienced a low mental score whereas 46 (43.0%) out of the 107 controls experienced a low mental score (OR = 2.8, 95%Cl 1.2 - 6.2) (Table 15).

There was no interaction between the SF36 and "consumption of regular Coca-Cola" (p=0.7).

Furthermore, the crude OR (2.4) and the MH_{OR} (2.6) were similar, giving no strong evidence for a confounding effect of the mental health status and the likelihood of reporting health complaints.

Regular Coca-Cola consumption					
Exposure		Cases	Controls	OR	(95%CI)
		(n = 31)	(n = 21)		
Sf36	yes	18 (58%)	8 (38%)	2.3	0.6 - 8.3
< median	no	13 (42%)	13 (62%)		
		No regular Co	ca - Cola consump	otion	
Exposure		Cases	Controls	OR	(95%CI)
		(n = 43)	(n = 107)		
Sf36	yes	29 (67.4%)	46 (43%)	2.8	1.2 - 6.2
< median	no	14 (32.6%)	61 (57%)		

Table 15 - Odds of experiencing a low mental health (SF36) stratified on the consumption of regular Coca-Cola, Other schools, Belgium 1999.

Crude_{OR} = 2.4; 95%CI: 1.3 - 4.5; MH_{OR} = 2.59, 95%CI 1.39 - 4.82

10. Scenario of the outbreaks in the schools

10.1.1 Scenario in Bornem

Students can only buy soft drinks at the school restaurant during the noon-break, which starts at 12:05'. Soft drinks are sold directly from the crate. On June the 8th some students complained the Coca-Cola purchased at the school restaurant, smelled and tasted bad. Some students drank the soft drink, some bottles were returned back half full and some of the bottles were replaced. Because there were so many students who had complaints about their Coca-Cola, the school stopped the sale. All soft drinks sold on the 8th of June at noontime came from a delivery of 20 crates done on the 8th of June during the morning, as the stock in school was nearly empty.

At 13:10' the classes restarted. Starting from 13:30' students from different classes with health complaints individually came to the secretariat, at 13:45' there were already more than 10 students with complaints. Most ill students had no contact with each other prior to going to the secretariat. Alerted by his secretariat, the director consulted the Medical School Inspection (MSI) to ask what to do. The MSI advised (by phone) to take all the students to hospital. Checking in every classroom, additional students with complaints were identified. With cars from the staff the students were brought to hospital where they had to wait in the corridor. In total 22 students were brought from school to hospital.

The link with the consumption was made very fast, because of the experience the school had with bad smelling Coca-Cola during the noon-break. According to the director all students with health complaints had drank Coca-Cola. Nevertheless, there were also many students who had consumed Coca-Cola and didn't have health complaints (5 crates of Coca-Cola were sold during the noon-break). Contact was made with Coca-Cola Antwerp to ask if they were aware of complaints the students had expressed.

Meanwhile the director from Coca-Cola Antwerp had come to the school where two crates out of

the remaining 15 were collected for examination.

In hospital a blood- and urine sample was taken from the students. Some of them received oxygen. At this moment some students were upset and frightened because of the blood control. All this happened before 14:50', the playtime of the other students.

At 15:50' the other students went home. The director made them feel at ease by saying that their friends were in the hospital, but that there were no major problems.

In the course of the evening another 11 students went from home to the hospital because of their health complaints. At that moment 33 students were hospitalised. At 19:00 18 students were dismissed, 15 (the worst cases) other remained hospitalised overnight.

The next day, Wednesday June 9th, all 33 students hospitalised received chest radiography. Also another 6 students who had some health complaints were taken to hospital. Overall 39 students had had contacts with a hospital service: 18 with the emergency unit (dismissed at 19 h.), 15 stayed overnight and 6 new cases had the chest radiography the next day. After the radiography, all students were dismissed from hospital and went to school. At school they briefly discussed about what had happened and then returned home.

On June 10th the majority of the students returned to school, but after half an hour some of them contacted the secretarial office again with health complaints (lack of concentration, tiredness). The director told them to return to their homes and to come back on Monday. On Monday, June 14th, all but 4 students returned to school (Those 4 students were not present at the day of the interview, nor was there any information on their health situation).

10.1.2 Scenario in Brugge

Students can buy canned soft drinks in tins on the playground (vending machine) during recreation time (between 10 and 10:10') or in the school restaurant during lunchtime.

The first pupil reported health complaints soon after recreation time (at 10:30), a second pupil between 10:30' and 10:45'. Before noon, 7 students stated to have health complaints. From the moment two students reported sick the 'nurse' contacted the hospital emergency services to bring the students to a hospital. The ambulances would visit the school 3 or 4 times to take sick students to hospital.

Based on the large media attention for the events in Bornem, the link with the consumption of soft drinks was rapidly made. The students with health complaints were asked if they had consumed soft drinks bought at the vending machine; they said they had consumed Coca-Cola light (in tins 33 cl.). Immediately after the first complaints the director stopped the selling of soft drink on the playground. He also contacted the Coca-Cola Company.

The 7 students with health complaints came from 5 classes of a different level. According to the director it was impossible that these students had had contact prior to the events since they all came directly from their classes at the moment of the complaints. The only thing in common was the fact that they had bought soft drinks on the playground.

Four students were dismissed from hospital in the course of the day

All the students taken to hospital could leave the hospital at evening. According to the director they all suffered from indigestion.

The students with complaints did not show a common characteristic; they were all 'normal' students with normal study results. One pupil – according to the director – faked his complaints.

10.1.3 Scenario in Harelbeke

At 1:30' p.m. on Friday 10th, two students with complaints came to see the director. They stated to suffer from head- and belly-pain. As usual, when students have health complaints, they spend

some time in the school sickbay (a small room with two beds). Around 3 o'clock another 4 students reported health complaints and were also taken to the sickbay. Worried about the increasing number of students with complaints, the director contacted a doctor (not the school doctor as he was absent). After a brief examination of the 6 students, the doctor gave an "antalgic effervescent tablet" and "MotiliumÒ". In the meantime another 3 students reported sick. The doctor contacted a hospital where alarm phase I was activated: 5 ambulances and the special medical urgency team were sent to the school. 13 students were taken to different hospitals in the neighbourhood. Later on, another 2 students were hospitalised (directly from home to a hospital).

The majority of the students reported to have health complaints came from only two classes. They showed no specific characteristics compared to the other students.

After 6 students reported being ill, the director searched for the cause. All six students were asked whether they had eaten hot meals in school. None of them had. Based on the events in Bornem, a link was made with the consumption of soft drinks. In Harelbeke, students are only allowed to by soft drinks during the noon-break in the restaurant. There are no automatic drink dispensers in the school. Students are allowed to bring soft drinks from home. From the 13 students having health complaints, 3 took (canned) soft drinks from home. The other 10 had bought soft drinks (coca and Fanta) at school during the noon-break.

Twelve out of 15 students temporarily hospitalised were dismissed on Friday-evening. The 3 others were dismissed the next day. According to the director this had nothing to do with the nature of the complaints of these three students but only with the policy of the hospital (St.Maarten Hospital). The next Monday, 3 students were again hospitalised. Two of them had gone to school on Monday morning, the other went directly from home to the hospital. On Thursday another three students were again hospitalised.

10.1.4 Scenario in Kortrijk

Around 2 p.m., during courses, two students with complaints came to see the director. They stated to suffer from headache, vomiting and abdominal complaints. Soon after, other students reported health complaints. Because it was obvious some students suffered from severe pain it was decided to contact the hospital and to bring the sick students to the hospital. Ten students were taken directly from the school to the hospital, two students went from home to the hospital (total number of initial cases: 12). Most of the students could leave the hospital soon. One pupil had to stay in the hospital and was still hospitalised moment of the investigation by the ISP.

The 12 cases came from different classes: 6 from one class (3rd year), 4 from two classes (4th year), one from one class (1st year) and one from one class (3rd year).

From 11 cases it is known that they consumed canned Coca-Cola and other soft drinks on the reference day. From these 11, seven students bought (one or more) canned Coca-Cola in school, 3 students bought their Coca-Cola in a shop outside, and one pupil brought the Coca-Cola from home. Since the 14th of June was a very hot day, it is plausible that the students consumed several cans of Coca-Cola during the day.

According to the director of the school, it was clear to him that one of the 12 students taken to hospital didn't suffer from any health complaint, and he knows another pupil as a more unstable person. This last pupil was dismissed soon after the hospital admission, but was again to be admitted to hospital a few hours later.

None of the students showed any specific study profile. All except one passed the examination without any problem. One pupil did not succeed, but the failure of particular student was not attributed to the incident of the 14th.

10.1.5 Scenario in Lochristi

On June 14th, before classes, the director telephoned to a hotline set up by Coca-Cola and asked about the safety of the drinks in the school's two vending machines. The Coca-Cola company told him that the company believed there was no real problem, but that he should remove all cans stamped on

the bottom with codes that included the letters DU, DV and DW. The school staff followed this instruction. Soft drinks were sold during the break starting from 10.30'.

Around 11 o'clock a few students from two different classes stated they had head and stomach complaints. As usual in such a case, it was decided they could spend some time in the corridor in order to recover. Around 11:15' the director contacted a doctor as the complaints didn't go away and other students had also come to the school office having the same complaints. It was decided to call for an ambulance to bring 4 students to the hospital. By the time the ambulance arrived, 6 students were considered to be really sick and should be brought to hospital. As usual when calling an ambulance, the police was alarmed automatically. Shortly after the arrival of the ambulance the police officer arrived. He decided that all students who stated to have complaints should be taken to hospital. In total, 37 students were taken to two hospitals. The majority of these 37 came from two classes, while the others came from different classes. The director, who didn't agree with the police officer, estimates that 20 students pretended to have complaints.

The majority of the students were soon dismissed of the hospital. Eight students had to spend one night in hospital, one pupil had to stay 2 nights.

The link with the consumption of soft drinks was made very fast (considering the contact the school had had with the Coca-Cola hot line). The students with health complaints were asked if they had drank soft drinks from the vending machine at school (they all said yes). At 11:30' the Coca-Cola hotline was contacted again by school, stating students had become ill. The Coca-Cola official now told him that Fanta (or BONAQUA) cans, as well as any cans labelled DX and DP had to be removed.

11. Biological parameters and other examinations

11.1 Bornem

It was regrettable that, although blood and urine sample from students of Bornem were collected, there was no evidence of any analysis or at least no results of the analysis could be obtained. We asked for some analysis on frozen blood sample, but the results were difficult to interpret.

Radiography of the chest was performed for 31 cases and all were normal.

One electrocardiograph was performed for one student because of a tachycardia, identifying a sinusal tachycardia.

An electromyography was performed for one student because of myalgia in the legs and it was normal.

One student out of the 11 of whom temperature was taken, had a t° exceeding 38°C. This t° could be attributed to an upper respiratory infection.

The pulse of 29 cases was measured (mean 92bt/mn, min 64bt/mn, max 136bt/min). Five cases had a tachycardia (pulse > 100bt/mn).

The blood pressure was collected for 31 cases. The systolic blood pressure ranged from 90 mm Hg to 150 mm Hg (mean = 120). Two cases had a systolic blood pressure superior to 140 mm Hg. The diastolic blood pressure ranged from 50 mm Hg to 90 mm Hg (mean = 71). Ten cases had a diastolic blood pressure inferior to 70 mm Hg.

11.2 Other schools

Biological investigations were performed on blood sample of 56 (74.66%) students from the other schools. All results were normal.

Urine examination was performed on 17 samples, 7 were negative and on 10 no information was obtained.

Stool examinations (bacteriological, virological) were performed for 10 cases and all results were

negative.

Electrocardiography was performed for 6 students and there were all normal.

Electroencephalography was performed for 5 students. Four of them were normal. One patient had abnormal electroencephalograph but the abnormality was attributed to an unspecified cause.

Eleven students out of the 37 of whom temperature was taken had a t° > 37°5 C. There was no biological sign of infection. Clinical examination was normal, except a flush for 3 of them.

The pulse of 40 cases was collected (mean 88bt/mn, min 59bt/mn, max 125bt/min). Five cases had a tachycardia (pulse > 100bt/mn).

The blood pressure was collected for 36 cases. The systolic blood pressure ranged from of 90 mm Hg to 160 mm Hg (mean of 95). Two cases had a systolic blood pressure superior to 140. The diastolic blood pressure ranged from 40 mm Hg to 90 mm Hg (mean of 72). Eleven cases had a diastolic blood pressure inferior to 70 mm Hg.

12. Delay between the time of beverage and the onset of the disease

12.1 Bornem

In Bornem, all cases but 3 drank their beverage between 12h00 and 12h30. This was the unique time at which beverages were available. Two of the students notified 17h30 as the time of beverage and one notified 8h00 a.m. There were 3 data missing.

The median of the delay between the time of the beverage and the onset of the disease was 3 hours, 2 hours and half for the girls (min. 30', max. 20h30') and 3 hours for the boys (min. 30', max. 24h30') (figure 6).

Figure 6: Number of cases by delay between the onset of the disease and the time of beverage consumption, Bornem, Belgium 1999.



12.2 Other schools

In the other schools, the median of the delay between the time of the beverage and the onset of the disease was 2 hours, 1hours and half for the girls (min. 30', max.08h00') and 30 minutes for the boys (min. 30', max. 4h00').

Figure 7: Number of cases by delay between the onset of the disease and the time of beverage consumption, Other schools, Belgium 1999.



13. Toxicological analysis on blood and urine samples

13.1 Bornem

Toxicological analysis was performed on blood sample of 8 (25%) patients of Bornem. Traces of caffeine were found for all of them with doses smaller than expected from eventual treatments with caffeine-containing medication (6 - 20).

No urine analysis was performed.

Blood and urine samples were sent to the toxicological lab at the UZA in Antwerp. No printed information was obtained nor by the IPH, nor by the treating physicians. It is unclear how many samples were analysed and what analyses were done. It is equally unclear what toxic compounds were searched for.

13.2 Other schools

Toxicological analysis was performed on blood sample of 38 (61.3%) patients of the other schools. Traces of caffeine and cotinine were found for 1 patient with dose smaller than the expected dose under treatment (6 - 20). Results were negatives for 27 patients. There were missing data for 10 patients.

Toxicological analysis was performed on urine of 8 patients. Three results were negative. There were traces of caffeine, nicotinine and amphetamine for 2 samples. There were missing data for 3 patients.

14. Cumulative number of cases among the students (cases + controls) who have consumed beverages

Figure 8 represents the cumulative number of cases by gender and schools, among students (cases + controls) who had consumed beverages. Time on axis represents the delay between beverage consumption and the onset of the disease.

In Bornem, the risk to be ill after consumption was similar for girls and boys. Cumulative incidence rose sharply in the early phase for both genders. Thirty percent of boys and 45% of girls were sick before a delay of 3 hours (Figure 8).

In the other schools, girls were more likely to become ill than boys and cumulative incidence rose sharply for females in the early phase whereas for male it rose moderately. Twenty percent of boys versus 40% of girls were sick before a delay of 4 hours (Figure 8).

Figure 8: Cumulative number of cases who have consumed beverages, by gender and schools, Belgium 1999.



* Delay between beverage consumption and the onset of the disease.

15. Cluster in classrooms

15.1 Bornem

In Bornem, 20 cases out of the 37 were grouped in 4 classrooms (6 cases in 2 classes and 4 in 2 classes). The other 17 cases were spread over 9 classrooms.

Among the 12 first cases, there were 2 groups of 3 students in the same 2 classrooms and the 6 other were spread in 6 different classrooms.

Seven cases were mentioned more than 2 times as an "ill friend" by the other cases.

15.2 Other schools

In Brugge, 5 cases out the 11 were grouped in 2 classrooms. The other 6 cases were spread in 6 classrooms. One case was mentioned 4 times as an "ill friend".

In Harelbeke, 11 cases out the 17 were grouped in 2 classrooms (1 classroom grouped 4 cases, one other grouped 7 cases). Six cases were mentioned more than 2 times as an "ill friend" by the other cases.

In Kortrijk, 1 classroom grouped 3 cases out the 12 and the 9 other were spread in 9 classrooms. Three cases were mentioned more than 2 times as an "ill friend" by the other cases.

In Lochristi, 32 out the 35 cases were grouped in 6 classrooms (3 cases in 2 classrooms, 5 in 1 class, 6 in 2 class and one classrooms grouped 9 cases). Eight cases were mentioned more than 2 times as an "ill friend" by the other cases.

16. Toxicological, bacteriological, virological analysis of the beverages

The Coca-Cola Company Northwest Europe Division asked for toxicological analysis on sample of beverages to:

- 1. The Coca-Cola Company laboratory, Atlanta
- 2. The Netherland Voeding, Organisation for Applied Scientific Research (TNO)

- 3. The National Medical Services (NMS), U.S.A.
- 4. The Analyses Controles expertises (ACE), France

Comments and health risk assessment based on the above analysis and asked by Coca-Cola Company were made by:

- 1. The Danish Toxicology Centre (DTC)
- 2. The Research Institute of Toxicology (Utrecht University)
- 3. The Fraunhofer Institute (Institute Toxikologie und Aerosolforschung, Hannover)

The Food Inspection of the Ministry of Public Health of Belgium ordered for laboratory analysis on beverages coming from the different schools concerned. No technical descriptions of the performed analyses were provided.

Two substances were incriminated to be responsible for an off odour:

- 1. Carbonyl sulphide (COS) and hydrogen sulphide (H₂S) in the Coca-Cola bottles sent to the school of Bornem and supplied by the Antwerpen production site.
- 2. P-chloro-m-cresol (PCMC) also known as 3-methyl-4-chlorophenol on the surface of soft drink cans sent to the other schools and supplied by the Dunkerque production site.

16.1 Hydrogen sulphide (H₂S) and carbonyl sulphide (COS)

Upon the sensory analysis a clear off-odour was established in suspected sample of Coca-Cola from 0.2 I glass bottles from the Antwerp production site, production dated June 4, 1999.

The analyses performed by gas chromatography in combination with a sniffing technique (GC-SNIFF) allowed to detect the compound (H_2S , COS) responsible for this off-odour, but the concentration was below the limit of detection for identification by gas chromatography and mass spectrometry (GC-MS) (annex 4).

Experts concluded, "levels of hydrogen sulphide of 8-17 μ g/l in Coca-Cola bottles are likely to produce a foul odour, which itself may bring about anxiety and stomach upset, and perhaps other anxiety symptoms such as profuse sweating. Other than this, no adverse health effects could be expected from the present, single exposure." (annex 4).

16.2 P-chloro-m-cresol (PCMC)

TNO employees with experience in sensory investigation confirmed a deviating odour characterised as "medicine like", outside the can. By GC-MS the compound responsible for the odour was identified as chlorocresol.

Experts concluded, "PCMP in the amount of 1.5µg externally on Coca-Cola cans is low compared to the levels of PCMC found in pharmaceuticals and cosmetics and background levels of phenolic compounds with which human beings are normally exposed. In persons already sensitised to PCMC, the risk of skin reactions following contact with cans contaminated with 0.4µg/can is considered to be low. PCMC was not detected in the liquid portion".

Symptom expected with PCMC is eyes and skin irritation that were not the major symptoms described by the students. Only few students complained for eye irritation.

16.3 Bacteriological and virological analysis

Microscopic inspection and culture did not reveal the presence of viable micro-organisms in the sample of drinks taken in relation to the cases of Bornem.

Light microscopy magnification 1000 times did not show parasites.

17. Media information

The event of Bornem was widely propagated by the media (radio, television, and paper) the first day of the outbreak and the following days. The information was spread both in Flemish and French media. As the event occurred in the Flemish region, the news was more widely diffused in this region.

18. Discussion

This study showed several arguments for both hypotheses.

18.1 Bornem

18.1.1 Coca-Cola Company products hypothesis

The Coca-Cola consumption hypothesis was supported by a high risk of illness for students exposed to regular Coca-Cola consumption. A similar risk for girls and boys, the lack of classical MSI trigger amplifier present or occurring "in line of sight" at least for the 12 first cases (the students did not see each other getting ill), the lack of other risk factors, i.e. SF36 and the lack of interaction with the SF36 also supported this hypothesis in Bornem.

The major symptoms were more important for the first 12 cases. Doctors in the emergency noted that those first cases were sicker (pallor and weakness) than the following. No clusters within a classroom were identified among the first cases, marking the lack of occurring "in line of sight". In Bornem, the risk to be ill was similar for girls and boys and the cumulative incidence curve rose sharply in the early phase for both genders.

The off-odour of the regular Coca Cola noted by the students was confirmed by the toxicological analysis, H_2S and COS were identified as the responsible compounds.

Even with levels of compounds below the lowest observed adverse effect level (LOAEL) (annex 4), symptoms of the students were consistent with the symptoms expected at a significant level of COS or [5] and several questions remain with only partial answer or no answer at all:

 In 1962, Hall noted water carbonated with CO₂ containing COS produced detectable H₂S some hours later, becoming stronger and disappearing after a few days [6]. All toxicological analyses were performed several days after the production day of the Coca-Cola from Antwerp. At that time, it is likely that if there existed detectable levels of H₂S on the day of consumption, the performed analyses may

have come too late to identify high levels of H₂S: the analyses only identified the residual

concentrations. What were the expected levels of COS and H_2S at the moment of the consumption? The exact kinetic curve is difficult to reconstruct, but building on the information of the report on the determination of COS concentration in carbon dioxide for quality control purpose [6], there was some increase in COS levels on the alleged production day (June 4th) of the bottles consumed in Bornem.

- 2. The average delay of marketing the Coca-Cola products is 3 to 4 weeks. Since there was little or no more products stocked because of an increase in sales as a result of a game allowing to win a GSM, the glass bottles of Coca-Cola were delivered in Bornem 4 days after the production. This delay was the most adequate time for a peak of COS and H₂S at the time of the consumption of the beverages by the students. Were the bottles of the same production run from Antwerp spread with the same delay to other site of consumption sites? Plastic bottles take much longer period to reach the consumers, allowing eventual COS and H₂S contamination to evaporate.
- Experts concluded that eventual toxic levels for COS and H₂S would require a substantial higher concentration than the one detected. Yet, little is know about the potential for smaller toxic doses for children, or about different toxicity levels through ingestion or inhalation.

Experts at the Danish Toxicology Centre (DTC) concluded, "In the evaluation of the results, it is essential to know in detail the association between the samples taken for analysis and the

suspected products to cause the illness. This detail information has not been available to the DTC at the time of writing this report, and therefore the value of the negative results will not be discussed further".

18.1.2 MSI hypothesis

Other arguments support a mass sociogenic illness in Bornem [2,3, 4].

The high risk of illness associated with the exposure to Coca-Cola consumption did not allow concluding to a toxic effect by the beverage.

The identified gas in the Coca-Cola could be a trigger factor and responsible for anxiety, stomach upset, and perhaps other anxiety symptoms. This hypothesis could be reasonable for the cases following the first cases. One can imagine that students probably carefully open the bottles after they heard of the first cases complain about the odour.

Symptoms were non-specific, but it was regrettable that collected blood sample were not analysed.

Classical risk factors of MSI were also present. The outbreak occurred in a school with a high proportion of teenager girls. The context of stress caused by the food security scare following the dioxine crisis, the upcoming elections and end examinations were cumulative risk factors.

The absence of toxicological confirmation of compounds responsible for toxicity is also in favour of a MSI, but as we saw above, some questions need more investigation.

18.2 Other schools

18.2.1 Coca-Cola Company products hypothesis

Even if the association with regular Coca-Cola consumption was weaker than in Bornem, it remained strong (Or = 5.5; 95%Cl 2.4 - 13). Cases were also more likely to have consumed other beverages (Fanta and Coca-Cola light). Toxicological analysis revealed low concentration of p-chloro-m-cresol on the exterior of the cans, that explain a bad smell and taste notified by a few students.

18.2.2 MSI hypothesis

There are several arguments in favour of the MSI hypothesis.

The association with Coca-Cola is not focused on one particular drink (Coca-Cola regular), but also present with consumption of other Coca-Cola beverages. Therefor, the association with Coca-Cola is not focused on one particular production site, but implicating two different production sites (Dunkerque, Gent). Different products and different production sites make a toxic cause less likely.

Classical MSI risk factors [2,3,4] were present:

- Girls were more likely to be ill than boys
- The outbreak occurred in schools setting
- Teenagers were concerned
- Variable and non specific symptoms
- No consistency between observed symptoms and expected symptoms if there was a toxicity of the methyl-cresol [5]
- The off odour of the methyl-cresol could be a trigger factor
- Context of stress: food security, dioxin crisis, elections days, schools end examination
- Role of media (radio, television, and paper): widely diffusion of the incident of Bornem before the second and following outbreak occurred in Brugge.
- Concentration of methyl-cresol below the LAOEL

 Clusters in classrooms were identified at least in 2 schools (Lochristi and Harelbeke); clusters in a classroom would satisfy the classic requirement for MSI to be amplified when occurring "in line of sight"

19. Limitations

The case control study was performed under extreme time-pressure (set up and completing the questionnaire, entering and analysis data in less than one week). There was no time to search for specific tools for testing MSI hypothesis. Questions on SF36 scores addressed the feeling of the students at the moment of the incident and they did measure neither the personality structure nor the mental health.

A delay of 15 days between the start of the incident (first outbreak in the first school) and the investigation could be responsible for a recall bias affecting the answers on symptoms, the consumption time of beverages or the time of the onset of the disease.

The results of this study need to be confronted to toxicological analysis of beverages. The lack of clear answer concerning the analysis done on the Coca-Cola consumed in Bornem and the imprecision of the kinetic curve of the incriminated products and it concentration during the consumption are major deficiency.

This study only included the cases occurring in the schools, while many other cases occurred in the community.

20. Conclusion

Both hypotheses are not mutual exclusive but could be associated.

In Bornem the association with the Coca-Cola consumption is clearly established. The contamination of COS and H_2S of Coca-Cola products could be a plausible explanation. More toxicological investigations should have been completed in order to prove or to reject the hypothesis of toxicity of the COS and H_2S .

In the other schools, arguments are more strongly in favour of MSI phenomena. This is enhanced by the conclusion of the French report concerning French cases who were exposed to the beverages provided by the same site production (Dunkerque) as the other schools [7]. The contamination of the Coca-Cola products by the P-chloro-M-cresol is not regarded as a plausible explanation.

21. Recommendations

21.1 Recommendation specific to the study

The lack of blood and urine sample analysis for the cases of Bornem did not allow to observe a modification of the biological parameters. More objective medical result should have been obtained from blood and urine sample analysis, avoiding lack of information.

As the Ministry of Public Health was already heavily implicated in the Dioxine crisis, the public measures for withdrawing the implicated products were insufficient and the Coca-Cola Company itself performed nearly all soft drink analyses. It would have been better to have all analyses of the suspected products performed by neutral laboratories.

Implication of the Unit of Epidemiology came too late. As the IPH was called nearly 2 weeks after the first outbreak, we recommend a sooner involvement of the epidemiological tool in such situation.

Tools for exploring a mass sociogenic illness should be improved. Several MSI episodes already occurred previously in Belgium, and are likely to re-occur.

21.2 General recommendation on the management of such events

The identified problems during the investigation show the need for more co-ordination between all the partners (Ministry of Public Health, toxicologist, physicians, laboratory and poisoning call centre, epidemiologists) when such events occur.

As in many other countries, a central intervention epidemiology unit should receive the initial request to investigate. Intervention epidemiologists are medical specialists trained to respond and co-ordinate these investigations. The Unit of Epidemiology at the Scientific Institute of Public Health has the resources and the capacity to develop this response and co-ordination, but lacks the mandate to develop intervention epidemiology. The mandate includes a clear, legally defined, task to tackle crises in public health. This mandate should be issued and supervised by all the different (public health) authorities. To allow an immediate response, a contact person within each of these authorities should be defined. To allow supervision, a supervisory body should be installed, a role which could be taken by the High Council of Health.

Providing such a development, this intervention epidemiology unit should be able to address future management problems as the ones encountered

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23. Annex 1



Onderzoek naar oorzaken van ziekte episodes in scholen, juni 1999

23.1.1 DATUM:/...../...../

SCHOOL:

KLAS:

DOSSIERNUMMER:

23.1.2

23.1.3

23.1.4

INLEIDING

We zijn werkzaam als onderzoekers op de afdeling Epidemiologie van het Wetenschappelijk Instituut Volksgezondheid. In het begin van deze maand zijn er enkele jongeren ziek geworden in je school.

Deze ziekte wordt in verband gebracht met het gebruik van frisdranken. Verschillende laboratoriumonderzoeken hebben nog geen duidelijke verklaring gegeven. Om toch beter te begrijpen wat er gebeurd is willen we je enkele vragen stellen over je voedingsgewoonte en je gezondheid. De meeste vragen kan je met een eenvoudige ja of neen beantwoorden. Als je het antwoord niet meer weet dan kan je dit ook zeggen.

Alhoewel straks naar je naam en zo zal gevraagd worden zullen alle gegevens anoniem bewaard en geanalyseerd worden.

Indien je op een vraag niet wenst te antwoorden dan kan je dit ook aangeven.

Voor verdere vragen kan je terecht bij:

Dr. Frank Van Loock Wetenschappelijk Instituut Volksgezondheid Afdeling Epidemiologie Juliette Wytsmanstraat 14 1050 Brussel

tel. 02/642.50.26 (50.37) fax. 02/642.54.10

Demografische gegevens

Naam		Voornaam
25.1.1.1.1 Straat		N°
Postcode		Stad
Telefoon		
Geboortedatum		Geslacht M V
Woon je thuis samen me moeder vader zus broer	et ja ne ja ne ja hoeveel ne ja ne ne hoeveel	e e e

Naam huisarts

VRAGENLIJST

- 26.1.1 Ik zal je eerst enkele vragen stellen over je voedingsgewoonten
- 26.1.1.1.1 V1.Hoeveel maal per week neem je ontbijt? dagen
- V2. Hoeveel maal per week neem je een middagmaal? dagen
- V3. Hoeveel maal per week neem je een avondmaal? dagen

V4. Hoe vaak eet je een tussendoortje zoals koekjes, chocolade, bonbons, gebak, snoep enz?



V5. Hoe vaak drink je gesuikerde frisdranken zoals cola, limonade, softdrink, icethee, fruitsap, enz?



V7. Eet jij s'middags op school ?

Ja	Warme maaltijd aangeboden door de school
	Koude maaltijd aangeboden door de school
_	Koude maaltijd meegebracht van thuis Waar eet je dan
Neen	(Ga naar V9)

V8. Wat drink je NORMAAL tijdens de maaltijd op school ?



V9. Koop je soms frisdrank OP SCHOOL :

26.1.2.1.1.1	Restaurant	Automaat	Verkooppunt
Nooit of bijna			
1-2 maal per week			
3-5 maal per week			
6-7 maal per week			
2 of meer maal per dag			

Opjuni zijn er leerlingen op jullie school ziek geworden

V.10. Was je vriend / in één van hen?

	Ja Ja	WIE (max twee namen, voor-	achternaam)
	Neen		
V11 W	as jij één van hen ?		
	Ja (Ga naar V13)		
	Neen		
V12 W	as jij dan ziek op een a	ndere dag?	
	☐ ja : datum /	/	
	neen (Ga naar vra	aag V27)	
V13 W	eet je nog hoe laat de z	iekte begonnen is ? (zie lijst)	
	uur		
V14 W	eet je nog waar in je lic	haam de ziekte begonnen is :	

(plaats van lichaam)

V15 lk zal je enkele problemen opsommen die je tijdens deze ziekteperiode kan gehad hebben. Kan je telkens aangeven of je dit probleem had of niet, of weet je het niet meer? Als je er had kan je ook zeggen hoe lang het probleem duurde ?

Symptoom	JA	NEEN	Weet niet	Duur (dag/uren)
Koorts > 38°C				
Misselijkheid				
Braakneigingen				
Braken				
Buikpijn				
Diarree				
Bloederige stoelgang				
Beven				
Hoofdpijn				
Ongemakkelijk voelen				
Evenwichtsstoornissen				
Andere (Omschrijf)				

V15 Weet je nog welk van deze problemen je het meest stoorde of van welk probleem je het meest last had? (1 probleem)

26.1.2.1.2 V16 Hoe lang ben je ziek geweest?

..... (dagen/uren)

V17 Heb je een dokter geconsulteerd in deze ziekteperiode en/of ben je opgenomen in een hospitaal ?



neen (Ga naar V20)

V18 Kan je aangeven welke dokter(-s) je geconsulteerd hebt en/of deze je medicatie heeft voorgeschreven ?



datum spoedgevallen// medicatieJaNeen
Naam ziekenhuis
hospitalisatie
Naam dienst
Naam ziekenhuis :
Duur hospitalisatie :dagen /uren
V19 Weet je nog of de dokter laboratoriumtesten heeft aangevraagd :
Laboratoriumtest van Ja Neen Weet niet
Laboratoriumtest van urine:
Laboratoriumtest van stoelgang:
V20 Ben je nadien hervallen van deze ziekte ? Geef de datum aan waarop je bent hervallen. (vb: thuis en terug naar het ziekenhuis of in school en terug ziek of in ziekenhuis)
☐ Ja datum _/_/_
Neen (Ga naar V23)
V21 Kan je aangeven welke dokter(-s) je geconsulteerd hebt en/of deze je medicatie heeft voorgeschreven ?
datum huisarts _/_/_ medicatie Ja Neen
datum medicatie Ja Neen
datum medicatie \Box_{Ja} Neen
Naam ziekenhuis
Naam ziekenhuis
Naam ziekenhuis

Duur hospitalisatie :dagen /uren

V22 Weet je nog of de dokter laboratoriumtesten heeft aangevraagd :

Laboratoriumtest van bloed:	Ja	Neen
Laboratoriumtest van urine:	Ja	Neen
Laboratoriumtest van stoelgang:	Ja	Neen

V23 Weet je nog of er buiten je medeleerlingen nog andere mensen in je omgeving rond het zelfde ogenblik als jij ziek zijn geweest (of geworden):

Thuis	:	wie
Andere	:	wie:
V24 Heb je medicatie genomen in de w	eek voor juni?	
Ja Welke medicatie ?		
Neen		
V25 Heb je medicatie genomen <u>de dag</u>	voorjuni?	
Ja Welke medicatie?		
Neen		
V26 Voel je je nu nog ziek ?		
Ja Omschrijf ziekte		
Neen		
V27 Rook je ?		
Ja elke dag		
Ja af en toe		
Neen		

V28 De volgende vragen gaan over hoe je je voelt en hoe het met je ging <u>de afgelopen 4</u> <u>weken</u>. Zou je bij elke vraag dat antwoord willen geven dat het best benadert hoe je je voelde. Hoe vaak gedurende de <u>afgelopen 4 weken</u> ?

Γ

Т

	Altijd	Meestal	Vaak	Sorr
Was je erg zenuwachtig?				
Zat je zodanig in de put dat niets je kon opvrolijken?				
Voelde je je rustig en ontspannen?				Г
Voelde je je somber en neerslachtig?				Г
Was je gelukkig?				Г

V29 (Voor meisjes alleen)

Was je de dag, dat de ziekte begon op de school, onwel (omwille je menstruatie)?

Ja



Kan je even terugdenken aan de dag dat je ziek werd of dat de ziekte begon in je school, namelijk opjuni. Aan de hand van de volgende fiches willen we proberen een beeld te krijgen van de FRISDRANKEN die je op die dag hebt gedronken EN DIT ZOWEL VOOR, TIJDENS ALS NA DE SCHOOLUREN.

We zullen dit op een gestructureerde wijze doen.

V30 Heb je op de dag dat je ziek werd of dat de ziekte begon in je school één of meerdere frisdranken gedronken?





Neen (de bevraging is beëindigd)

V31 Welke frisdranken en hoeveel van elk heb je die dag gedronken ? Om je te helpen kan je gebruik maken van de lijst van frisdranken die voorheen werd gebruikt.

Naam frisdrank ______ Aantal gedronken

Naam frisdrank	Aantal gedronken
Naam frisdrank	Aantal gedronken
Naam frisdrank	Aantal gedronken

Het aantal in te vullen fiches dient overeen te komen met het aantal gedronken frisdranken. Indien je 2 flesjes (of blikjes of bricks) gedronken hebt van frisdrank X en 1 flesje (of blikje of brick) van frisdrank Y dien je in totaal 2 + 1 = 3 fiches in te vullen.

FICHE IN TE VULLEN PER GEDRONKEN FRISDRANK EN PER CONSUMPTIE

Naam frisdrank :

Hoe laat heb je deze frisdrank gedronken ? Tijdstip : uur (ev. bij benadering)

26.1.2.1.2.1.1 Verpakking van deze frisdrank was

Glazen Fles



Blikje

Tetrabrick

Indien fles, welk type?

	0,2 L	0,33 L	0,5 L	1 L
plastic				
glas				

26.1.2.1.2.1.2 Waar heb je deze frisdrank aangeschaft ?



Meegenomen van thuis



neegenomen van truis



Bij de schoolautomaat

Bij andere automaat

In een winkel



26.1.2.1.2.1.3 Waar heb je deze frisdrank opgedronken ?



School

Heb je deze frisdrank bij een maaltijd (onbijt, middagmaal, vieruurtje, avondmaal) opgedronken?





Indien neen, heb je deze frisdrank gedronken ongeveer twee uur of langer na een maaltijd?



Neen

26.1.2.1.2.1.4 Heb je iets specifiek opgemerkt met deze frisdrank?



Smaak (Omschrijf)

Geur (Omschrijf)

Uitzicht (Omschrijf)

De verpakking (Omschrijf)

Annex 2

MINISTERIE VAN SOCIALE ZAKEN,

VOLKSGEZONDHEID EN LEEFMILIEU



WETENSCHAPPELIJK INSTITUUT VOLKSGEZONDHEID - LOUIS PASTEUR*

Afdeling Epidemiologie

Web site: www.iph.fgov.be/epidemio/

*voorheen INSTITUUT VOOR HYGIËNE

EN EPIDEMIOLOGIE

Dossiernummer:....

Epidemie in de scholen van

Bornem, Lochristi, Brugge, Harelbeke, Kortrijk

Medische gegevens van de in het ziekenhuis opgenomen leerlingen

Datum://		
Ondervrager:		
Ziekenhuis:		
Afdeling:		
Geneesheer:		
Naam:	Voornaam:	
Straat:	Nr.:	
Postcode:		Stad, gemeente:
Geboortedatum:	Geslad	cht:
Naam en adres van de behandelend	e geneesheer:	
Binnengebracht via:	ziekenwagen	eigen vervoer
Opnamedatum://	uur van opname:	
Doorverwezen door:	de huisarts	
	de school	
	op eigen initiatief	
Rede van opname:		
Objectieve symptomen bij opname	<u>ə:</u>	
	JA	
	NEEN	
	WEET NIET DUUR (mn/h)	
Koorts		
Temperatuur:°C		

Braakneigingen		
Braken		
Retrosternaal branderig gevoel		
Branderig gevoel in de maag		
	C	
Buikpijn		
Diarree		
Vastheid van de stoelgang		
Aantal defaecaties /dag		
Bloed in de stoelgang	Γ	
Hoofdpijn		
Beven		
Evenwichtsstoornissen		
Draaierigheid		
Bewustzijnsverlies		

_

Malaise/Lypothimie			
Polypnee			
Spierpijnen			
Asthenie			
Onwillekeurige bewegingen			
Tintelingen in de ledematen			
Zweten			
Hartkloppingen			
Gevoel koud/warm			
Andere tekens			
welke:			
27. Vitale parameters bij opname			
Hartrytme:(mn ⁻¹)			
Bloeddruk: Systolische(mmHg) Diastolische	e(mmHថ្	g)	
Ademhalingsfrequentie:(mn ⁻¹)	Arteriële zuurstot	fverzadiging :	
Tekens van shock:			

Glasgow:						
----------	--	--	--	--	--	--

Biologische parameters	(!! Referenti	<u>ewaarden vragen aan de labo's)</u>
Natrium:(m	ıEq/I) Kalium	:(mEq/l)
Chloor:(mE	q/l) Magnesi	um:(mEq/l)
Glycemie:	(mmol/l)	
Ureum: Cro	eatinine:	
Art. pH : PaO2:	(mmHg)	PaCO2:(mmHg)
Bicarbonaat:	(mEq/l) Sa(D2:
Witte bloedcellen:	(/	/ml) % PNN:
Hemoglobine:	(g/	dl) VGM:
Bloedplaatjes:		.(/ml) Reticulocyten:(/ml)
Haptoglobine:	Eo	sinofielen:(%)
SGOT:(U/L) S	GPT:	(U/L)
LDH:	GC	GT:
Bilirubine:		Lipase:
Creatine fosfokinase (CPK):	Prothrombine gehalte:
C Reactieve Proteine:		Fibrinogeen:
JA	NEEN	
Bloedkweek :		Resultaat:
Coprocultuur:		Resultaat:
Urine (CB):		Resultaat:
Lumbale.P.:		Resultaat:
ECG:		Resultaat:
Buikoverzicht:		Resultaat:
Thorax RX:		Resultaat:

EMG			Resultaat:
EEG			Resultaat:
Echografie			Resultaat:
Andere:			Resultaat:
Opsporen van	toxica (alle r	eslutaten I	<u>beschrijven zelfs de negatieve):</u>
Bloed :			
Resultaat:			
Urine			
Resultaat:			
Behandeling:			
Weerhouden o	liagnose:		
Advies van de a	arts in verband	d met de or	gaanaantasting:
Zeker 🔲 waa	arschijnlijk	mogelijk	onwaarschijnlijk
Argumenten:			
Datum van vert	rek://.		Duur van het verblijf:(uren/dagen)

Motief voor opname in een andere afdeling dan de spoedafdeling:

Andere opnames: JA INEEN Andere opname een vragenlijst invullen)

Annex 3

Dossiernummer:.....

Epidemie in de scholen van Bornem, Lochristi, Brugge, Harelbeke, Kortrijk

Opinie van de behandelende geneesheren

Vragenlijst t.a.v. de geneesheren

Datum:/...../..... Enquêteur: Ziekenhuis: Dienst: Geneesheer: Hoe werd u op de hoogte gebracht van de intoxicatie in de scholen?

Hoe werd het onthaal van de kinderen in het ziekenhuis georganiseerd ?

Beschrijf het gedrag van de leerlingen ?

Op basis van welke criteria werd tot een hospitalisatie overgegaan ?

Op basis van welke criteria werd beslist de patiënt enkele uren in observatie te houden ?

Werden de symptomens zoals braken, diarree werkelijk geobserveerd? Zo ja, preciseer:

Welke syptomen waren het meest frequent ?

Naam: Voornaam

Opinie van de arts in verband met het organisch karakter:

Zeker 🗖 vermoedelijk 🗖 Mogelijk 🗖 onwaarschijnlijk 🗖
Argumenten: